REMARKS

By the amendments presented, Claim1 has been amended to delete reference in the preamble of the claimed nasal composition as being "a low irritation nasal composition".

Also by the amendments presented, Claim 7 has been amended to depend from claim 6 rather than reciting its dependency from claim 5.

Also by the amendments presented Claims 7 and 27 have been amended to correct typographical errors in the use of "semicolons" rather than "commas" in the Markush groups recited in these claims.

Attached hereto is a marked-up version of the changes made to the claims as a result of the current amendments. The attached page is captioned **"Version with Markings to Show Claim Changes Made"**.

Upon entry of the amendments presented, Claims 1-9 and 20-30 remain in the application. No additional claims fee is due.

Invention Synopsis

The present invention is directed to respiratory tract compositions, particularly nasal compositions, which provide for the prevention and treatment of cold and influenza viruses, and which comprise a combination of pyroglutamic acid and a specifically defined organic acid wherein this combination is especially effective in these prevention and treatment processes.

It has been found that nasal compositions containing a combination of pyroglutamic acid and an organic acid having a pKa value of from about 3.0 to about 5.0 can provide a surface pH of the nasal cavity tissue to create a nasal environment that is hostile to cold and influenza-like viruses. Nasal cavities having a pH in the range of from about 3.5 to about 5.5, which is provided by the compositions of the present invention, have been found to deter viruses which can lead to respiratory tract viral infections that can result in cold and influenza like symptoms.

Formal Matters

a) Priority

The present application has been objected to under 35 U.S.C. 120 for Applicants' continuation-in-part claim of priority to Application Serial No. 09/421,131 which was filed on October 19, 1999. The Examiner contends that Application Serial No, 09/421,131 fails to provide sufficient disclosure for nasal compositions comprising pyroglutamic acid and a metal salt as described by Applicants, and methods of using such compositions, therefore, Applicants' continuation-in-part claim of priority to Application Serial No. 09/421,131 is invalid and the effective priority date for the examination of the present application is October 19, 2000. Applicants respectfully traverse this objection.

Applicants disagree with the Examiner's assessment of Applicants' continuation-in-part claim of priority to Application Serial No. 09/421,131. Applicants submit that the claim of priority to Application Serial No. 09/421,131 is for that disclosed subject matter in Application Serial No.

09/421,131 which relates to similar subject matter as described by Applicants, for example, nasal compositions comprising pyroglutamic acid and a metal salt. Applicants specifically state that the present application is a continuation-in-part of prior Application Serial No. 09/421,131, which indicates that the present application contains new matter that is not disclosed in Application Serial No. 09/421,131, notwithstanding Application Serial No 09/421,131 disclosure that its compositions are essentially free of metal salts when the compositions contain pyroglutamic acid and claims in Application Serial No. 09/421,131 which are limited to an intranasal spray comprising pyroglutamic acid and a metal salt.

Applicants submits that the specification of Application Serial No. 09/421,131 provides sufficient disclosure for the limitations of Applicants' specification which relates to nasal compositions comprising pyroglutamic acid and a metal salt and, therefore, the present application is fully compliant with 35 U.S.C 120 in reciting that the present application is a continuation-in-part to prior Application Serial No. 09/421,131. For example, Application Serial No. 09/421,131 recites at page 4, lines 9-11, that this application further relates to "...methods for preventing and/or treating a common cold or associated respiratory disease in a mammal,...". Application Serial No. 09/421,131 further states at page 49, lines 14-23, that "compositions which contain pyroglutamic acid and which are essentially free of metal salts...are useful for ...preventing and/or treating a common cold or associated respiratory disease in a mammal... In each of these methods the area or surface to be treated may be selected from the group consisting of ...a nasal canal or passage..." At page 63 of Application Serial No. 09/421,131, Examples 39 and 40 exemplify an intranasal formulation comprising pyroglutamic acid. Application Serial No. 09/421,131 then recites in Claim 34 a personal kit comprising an intranasal spray that comprises pyroglutamic acid and a metal salt. Accordingly, Applicants have properly claimed the present application as a continuation-in-part of Application Serial No. 09/421, 131 for compliance with 35 U.S.C. 120. The objection of the present application as to its priority claim date is improper and, therefore, should be withdrawn.

b) <u>Rejection under 35 U.S.C. 112 (2nd paragraph)</u>

Claims 1-9, and 20-30 have been rejected under 35 U.S.C. 112 (2nd paragraph) as being indefinite for recitation in the preamble of Claim 1 of the claimed nasal composition as being "A low irritation nasal composition". Responsive to this rejection, Claim 1 has been amended to delete reference to the term "low irritation", thus obviating this rejection as it would apply to this amended claim. Applicants submit that the amendment to Claim 1 also applies to dependent or referred claims therefrom (Claims 2-9 and 20-30), thus this rejection is also obviated as it applies to Claims 2-9 and 20-30.

Claim 7 has also been rejected under 35 U.S.C. 112 (2nd paragraph) as being indefinite for reciting its dependency from Claim 5 rather than from Claim 6 to provide antecedent basis for more specifically defined descriptions of the claimed "mucoadhesive agent". Responsive to this rejection, Claim 7 has been amended to depend from Claim 6 rather than from Claim 5, thus obviating this rejection as it would apply to amended Claim 7.

c) Rejection under 35 U.S.C. 112 (1st paragraph)

Claims 1-9 and 20-30 have been rejected under 35 U.S.C. (1st paragraph) for an alleged failure to provide in the specification an enabling description for application of the compositions defined in these claims for the prevention of cold and influenza viruses. Applicants traverse this rejection.

Applicants submit that in the specification at pages 1-3 detailed description is provided to disclose several techniques to determine the efficacy of pharmaceutical compositions including nasal compositions in the prevention and treatment of cold and influenza viruses. For enablement, Applicants need to disclose to the skilled artisan how to make and/or use the compositions as claimed in Claims 1-9 and 20-30, and Applicants have done just that. Contrary to the Examiner's contention, to enable the skilled artisan how to make and/or use Applicants' invention does not require clinical data of an assessment of the claimed compositions recited in Claims 1-9 and 20-30. Applicant's specification provides sufficient description of its compositions as well as sufficient descriptions of suitable techniques that can be used to determine the efficacy of these compositions in the prevention and treatment of cold and influenza viruses. Accordingly, this rejection of Claims 1-9 and 20-30 for insufficient disclosure in the specification as to the prevention of cold and influenza viruses is improper, and should be withdrawn.

Art Rejections

a) Rejection under 35 U.S.C. 102

Claims 1-5 and 20-27 have been rejected under 35 U.S.C. 102 as being anticipated by Gangadharan et al. (U.S. Patent 5,643,582). The Examiner contends that Gangadharan et al. disclose moisturizers that can be administered nasally wherein the moisturizers comprise a combination of a humectant described as pyroglutamic acid and an organic acid such as benzoic acid, and as such Gangadharan et al. disclose Applicant's invention of a nasal composition comprising a combination of pyroglutamic acid and an organic acid including benzoic acid wherein the combination provides a surface pH of the nasal cavity tissue of from about 3.5 to about 5.5. Applicants respectfully traverse this rejection.

Gangadharan et al. disclose moisturizers which are suitable for rehydrating or maintaining hydration in skin and mucous membranes, and which comprise bioadhesives in combination with humectants and water complexing agents. Suitable humectants disclosed in the Gangadharan et al. reference include 2-pyrrolidinone-5-carboxylic acid salts (i.e., pyroglutamic acid salts). Gangadharan et al. further disclose that the moisturizers can also comprise other compositional ingredients that include preservatives such as benzoic acid and its salts wherein the benzoic acid compounds can also be used as acidulants, and that include pH adjusting acidulant materials to adjust the pH value of the composition between 3-5 for vaginal applications. Furthermore, Gangadharan et al. disclose that the moisturizes can be administered to different epithelial cells for dermis and mucous membrane contact including the epithelial cells of the buccal and nasal regions.

Gangadharan et al., however, fail to disclose a moisturizer in the form of a nasal composition that comprises a combination of a pyroglutamic acid and a specifically defined organic acid.

Applicants submit that to anticipate Applicants' Claims 1-5 and 20-27 the Gangadharan et al. reference should teach each and every limitation recited in these claims. Gangadharan et al. teach moisturizers that can be administered nasally, and that comprise a combination of a pyroglutamic acid salt and an organic acid such as benzoic acid. By contrast, Applicants' Claims 1-5 and 20-27 are limited to a nasal composition that comprises a combination of a pyroglutamic acid and an organic acid including benzoic acid.

The applied Gangadharan et al. reference fails to teach the pyroglutamic acid limitation of Claims 1-5 and 20-27 and, therefore, fails to anticipate these claims. Accordingly, the rejection of Claims 1-5 and 20-27 as being anticipated by Gangadharan et al. is improper and should be withdrawn.

b) Rejection under 35 U.S.C. 103 over Davidson et al. in view of Szentmiklósi et al. and Gangadharan et al.

Claims 1-9 and 20-30 have been rejected under 35 U.S.C. 103 as being unpatentably obvious over Davidson et al. (U.S. Patent 6,080,783) in view of Szentmiklósi et al. (U.S. Patent 5,244,880) and Gangadharan et al. (U.S. Patent 5,643,582). The Examiner contends that it would have been obvious to incorporate the pyroglutamic acid disclosed in Szentmiklósi et al. or Gangadharan et al. into the zinc containing nasal composition of Davidson et al., to thereby realize Applicants' invention. Applicants respectfully traverse this rejection.

Davidson et al. disclose a viscous gel which is suitable for delivering zinc or another metal to the nasal membrane. The viscous gel of Davidson et al. comprises a carrier and preferably a zinc gluconate compound wherein the zinc gluconate produces concentrations of ionic zinc for delivery into the nasal cavity. Davidson et al. further disclose that the viscous gel has a viscosity in the range of from 5,000 to 20,00 centipoise to facilitate maintenance of the gel in the nasal cavity. Davidson et al., however, fail to disclose a nasal composition comprising a combination of pyroglutamic acid and an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0.

Szentmiklósi et al. disclose pharmaceutical and cosmetic compositions which comprise aqueous solutions of primycin and pyroglutamic acid. In addition to primycin and pyroglutamic acid, Szentmiklósi et al. disclose that the pharmaceutical or cosmetic compositions can optionally comprise other therapeutic actives such as antibacterial (e.g., oxolinic acid) and/or anti-inflammatory agents. The compositions disclosed in the Szentmiklósi et al. reference are further described as clear, stable aqueous solutions which are formulated as topically applicable pharmaceutical compositions and disinfecting cosmetic compositions. Szentmiklósi et al., however, fail to disclose a pharmaceutical composition in the form of a nasal composition, and certainly fail to disclose a nasal composition comprising pyroglutamic acid in combination with an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0.

Gangadharan et al. disclose moisturizers which are suitable for rehydrating or maintaining hydration in skin and mucous membranes, and which comprise bioadhesives in combination with humectants and water complexing agents. Suitable humectants disclosed in the Gangadharan et al. reference include 2-pyrrolidinone-5-carboxylic acid salts (i.e., pyroglutamic acid salts). Gangadharan et al. further disclose that the moisturizers can also comprise other compositional ingredients that include preservatives such as benzoic acid and its salts wherein the benzoic acid compounds can also be used as acidulants, and that include pH adjusting acidulant materials to adjust the pH value of the composition between 3-5 for vaginal applications. Furthermore, Gangadharan et al. disclose that the moisturizes can be administered to different epithelial cells for dermis and mucous membrane contact including the epithelial cells of the buccal and nasal regions. Gangadharan et al., however, fail to disclose a moisturizer in the form of a nasal composition that comprises a combination of a pyroglutamic acid and an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0.

Applicants submit that the combined disclosures of the Davidson et al., Szentmiklósi et al., and Gangadharan et al. references, in any combination, fail to realize Applicants' invention of Claims 1-9 and 20-30. None of these applied references teach a nasal composition comprising pyroglutamic acid in combination with an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0.

The Examiner contends that it would have been obvious to combine the pyroglutamic acid of Szentmiklósi et al. or Gangadharan et al. with the nasal composition of Davidson et al., to thereby realize Applicants' invention. Applicants disagree. Applicants submit that a nasal composition as taught by combining the Davidson et al. and Szentmiklósi et al. references may yield a nasal composition comprising a zinc compound in combination with pyroglutamic acid, but this combination of references fails to teach or suggest Applicants' nasal composition of Claims 1-9 and 20-30 which comprises pyroglutamic acid in combination with a specifically define organic acid. Davidson et al. nor Szentmiklósi et al. teach or suggest a nasal composition comprising Applicants' organic acid. Applicants further submit that a combination of the Davidson et al. and Gangadharan et al. references may result in a nasal composition comprising a zinc compound, a pyroglutamic acid salt, and an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0, but a combined disclosure of Davidson et al. and Gangadharan et al. would fail to teach or suggest Applicants' nasal composition comprising pyroglutamic acid in combination with an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0

Moreover, Applicants submit that there is no motivation to combine Szentmiklósi et al. with Davidson et al. to formulate a nasal composition as taught by Applicants, prima facie or otherwise. Szentmiklósi et al. fail to teach or suggest nasal compositions altogether and, therefore, provides no motivation for the skilled artisan to even look to Szentmiklósi et al. for nasal compositions comprising pyroglutamic acid and certainly not to combine Szentmiklósi et al. teachings with Davidson et al. to result in a nasal composition that is still deficient in the nasal composition taught by Applicants. Likewise, it is not prima facie obvious to combine Gangadharan et al. with Davidson

et al. because Gangadharan et al. teach in passing that his compositions can be administered nasally, but the Gangadharan et al. compositions comprise pyroglutamic acid salts, not pyroglutamic acid, and, therefore, combining Gangadharan et al. with Davidson et al. would sill not result in Applicants' invention of Claims 1-9 and 20-30 which is directed to a nasal composition comprising pyroglutamic acid.

In view of the foregoing remarks, it is submitted that the applied Davidson et al., Szentmiklósi et al., and Gangadharan et al. references, in any combination, would not obviously lead the skilled artisan to a realization of Applicants' invention of Claims 1-9 and 20-30, as amended. Accordingly the rejection of Claims 1-9 and 20-30 as being unpatentably obvious over Davidson et al. in view of Szentmiklósi et al. and Gangadharan et al. is improper, and should be withdrawn.

c) Rejection under 35 U.S.C. 103 over Elliott et al. in view of Gangadharan et al.

Claims 1-7 have been rejected under 35 U.S.C. 103 as being unpatentably obvious over Elliott et al. (U.S. Patent 5,905,062) in view of Gangadharan et al. (U.S. Patent 5,643,582). The Examiner contends that it would have been obvious, based on the disclosure of Gangadharan et al., to formulate a composition of Elliott et al. into a nasal composition, to thereby realize Applicants' invention. Applicants respectfully traverse this rejection.

Elliott et al. disclose liquid personal cleansing compositions which may be used in the form of foam bath preparations, shower products, skin cleansers, hand, face and body cleansers, and shampoos, and which optionally comprise a moisturizer such as L-proline (i.e., pyroglutamic acid). The liquid personal cleansing compositions of Elliott et al. are further described as having a pH of from about 4 to about 10. Elliott et al., however, fail to disclose nasal compositions, and certainly fail to disclose a nasal composition comprising a combination of pyroglutamic acid and an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0 wherein the combination of pyroglutamic and organic acids provides a surface pH of the nasal cavity tissue of from about 3.5 to about 5.5.

Gangadharan et al. disclose moisturizers which are suitable for rehydrating or maintaining hydration in skin and mucous membranes, and which comprise bioadhesives in combination with humectants and water complexing agents. Suitable humectants disclosed in the Gangadharan et al. reference include 2-pyrrolidinone-5-carboxylic acid salts (i.e., pyroglutamic acid salts). Gangadharan et al. further disclose that the moisturizers can also comprise other compositional ingredients that include preservatives such as benzoic acid and its salts wherein the benzoic acid compounds can also be used as acidulants, and that include pH adjusting acidulant materials to adjust the pH value of the composition between 3-5 for vaginal applications. Furthermore, Gangadharan et al. disclose that the moisturizes can be administered to different epithelial cells for dermis and mucous membrane contact including the epithelial cells of the buccal and nasal regions. Gangadharan et al., however, fail to disclose a moisturizer in the form of a nasal composition that comprises a combination of a pyroglutamic acid and an organic acid having a dissociation constant (pKa) value of from about 3.0 to about 5.0.

Applicants submit that the teachings of Elliott et al. in view of Gangadharan et al. would not obviously lead the skilled artisan to a realization of Applicants' invention of Claims 1-7. Both of these applied references, alone and in combination, fail to teach or suggest a nasal composition comprising pyroglutamic acid in combination with a specifically defined organic acid.

The Examiner contends that since Gangadharan et al. in passing describe a moisturizer that can be administered nasally, Gangadharan et al. provides the needed teachings and suggestions for the skilled artisan to modify the liquid personal cleansing compositions of Elliott et al. into a nasal composition. Applicants disagree. Gangadharan et al. may provide some teaching or suggestion to formulate a nasal composition comprising pyroglutamic acid salts, but certainly fail to teach or suggest a nasal composition comprising pyroglutamic acid. Moreover, there should be some teaching or suggestion in a reference itself in order for the skilled artisan to modify the reference to result in Applicants' invention of Claims 1-7. Elliott et al. fail to teach or suggest nasal compositions altogether, and provides no motivation for the skilled artisan to formulate Elliott et al.'s cleansing compositions into a nasal composition, despite the reliance on another reference teaching or suggestion of a moisturizer that can be administered nasally. Furthermore, the attempt to formulate Elliott et al.'s cleansing compositions into a nasal composition would still be deficient in the nasal composition comprising Applicants' organic acid, Elliot et al. fail to teach or suggest any type of composition comprising Applicants' defined organic acid component.

Accordingly, the teachings of Elliot et al. in view of Gangadharan et al. fail to obviously lead the skilled artisan to a realization of Applicants' invention of Claims 1-7, as amended. The rejection of these claims as being unpatentably obvious over Elliott et al. in view of Gangadharan et al. is improper and should, therefore, be withdrawn.

Conclusions

Applicants have made an earnest effort to place their application in proper form and to distinguish their claimed invention from the applied prior art. WHEREFORE, reconsideration of this application, entry of the amendments presented, withdrawal of the rejections under 35 U.S.C. 120, 35 U.S.C. 112 (1st and 2nd paragraphs), and 35 U.S.C. 102 and 103, and allowance of Claims 1-9 and 20-30 are respectfully requested.

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Version with Markings to Show Claim Changes Made

Claim 1. (Amended) A [low irritation] nasal composition for prevention and treatment of cold and influenza viruses comprising pyroglutamic acid and an organic acid having a dissociation constant (pKa) value from about 3.0 to about 5.0 wherein the combination of said pyroglutamic and organic acids provides a surface pH of the nasal cavity tissue from about 3.5 to about 5.5.

Claim 7. (Amended) The composition according to claim [5] 6 wherein the mucoadhesive agent is selected from the group consisting of carboxypolymethylene[;], carboxyvinyl polymers[;], homopolymers of acrylic acid crosslinked with an allyl ether of pentaerythritol[;], homopolymers of acrylic acid crosslinked with an allyl ether of sucrose[;], homopolymers of acrylic acid crosslinked with divinyl glycol[;], and mixtures thereof.

Claim 27. (Amended) The composition according to claim 26 wherein the mucoadhesive agent is selected from the group consisting of carboxypolymethylene[;], carboxyvinyl polymers[;], homopolymers of acrylic acid crosslinked with an allyl ether of pentaerythritol[;], homopolymers of acrylic acid crosslinked with an allyl ether of sucrose[;], homopolymers of acrylic acid crosslinked with divinyl glycol[;], and mixtures thereof.